



SEQUENCE LISTING

<110> McKeon, F.
Kayako, K.
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<120> CALCIPRESSINS: ENDOGENOUS INHIBITORS OF CALCINEURIN,
USES AND REAGENTS RELATED THERETO

<130> HMV-048.01

<140> 09/575,580

<141> 2000-05-22

<150> 60/135,431

<151> 1999-05-21

<150> 60/161,195

<151> 1999-10-22

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<170> PatentIn Ver. 2.1

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<211> 2484

<212> DNA

<213> Homo sapiens

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<212> DNA
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 <211> 198
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 <213> Mus musculus

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 35 40 45
 Lys Ser Phe Lys Arg Val Arg Ile Asn Phe Ser Asn Pro Leu Ser Ala
 50 55 60
 Ala Asp Ala Arg Leu Arg Leu His Lys Thr Glu Phe Leu Gly Lys Glu
 65 70 75 80
 Met Lys Leu Tyr Phe Ala Gln Thr Leu His Ile Gly Ser Ser His Leu
 85 90 95
 Ala Pro Pro Asn Pro Asp Lys Gln Phe Leu Ile Ser Pro Pro Ala Ser
 100 105 110
 Pro Pro Val Gly Trp Lys Gln Val Glu Asp Ala Thr Pro Val Ile Asn
 115 120 125
 Tyr Asp Leu Leu Tyr Ala Ile Ser Lys Leu Gly Pro Gly Glu Lys Tyr
 130 135 140
 Glu Leu His Ala Ala Thr Asp Pro Thr Pro Ser Val Val Val His Val
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 Cys Glu Ser Asp Gln Glu Asn Glu Glu Glu Glu Glu Met Glu Arg
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 Met Lys Arg Pro Lys Pro Lys Ile Ile Gln Thr Arg Arg Pro Glu Tyr
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 Thr Pro Ile His Leu Ser
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<210> 5
 <211> 242
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 35 40 45
 Leu Thr Asp Phe Ser Asp Leu Pro Asn Ser Leu Phe Ala Cys Asn Val
 50 55 60
 His Gln Ser Val Phe Glu Glu Glu Glu Ser Lys Glu Lys Phe Glu Gly
 65 70 75 80
 Leu Phe Arg Thr Tyr Asp Glu Cys Val Thr Phe Gln Leu Phe Lys Ser
 85 90 95
 Phe Arg Arg Val Arg Ile Asn Phe Ser His Pro Lys Ser Ala Ala Arg
 100 105 110
 Ala Arg Ile Glu Leu His Glu Thr Gln Phe Arg Gly Lys Lys Leu Pro
 115 120 125
 Leu Tyr Phe Ala Gln Val Gln Thr Pro Glu Thr Asp Gly Asp Lys Leu
 130 135 140
 His Leu Ala Pro Pro Gln Pro Ala Lys Gln Phe Leu Ile Ser Pro Pro
 145 150 155 160
 Ser Ser Pro Ser Val Gly Trp Lys Pro Ile Ser Asp Ala Thr Pro Val
 165 170 175
 Leu Asn Tyr Asp Leu Leu Tyr Ala Val Ala Lys Leu Gly Pro Gly Glu
 180 185 190
 Lys Tyr Glu Leu His Ala Gly Thr Glu Ser Thr Pro Ser Val Val Val
 195 200 205
 His Val Cys Asp Ser Asp Met Glu Arg Glu Glu Asp Pro Lys Thr Ser
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 225 230 235 240
 Gly His

<210> 6
 <211> 192
 <212> PRT
 <213> Homo sapiens

<400> 6
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Val Arg Ile Asn Phe Ser Asn Pro Lys Ser Ala Ala Arg Ala Arg Ile
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 Glu Leu His Glu Thr Gln Phe Arg Gly Lys Lys Leu Lys Leu Tyr Phe
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 Ala Gln Val Gln Thr Pro Glu Thr Asp Gly Asp Lys Leu His Leu Ala
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 Pro Pro Gln Pro Ala Lys Gln Phe Leu Ile Ser Pro Pro Ser Ser Pro
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 Pro Val Gly Trp Gln Pro Ile Asn Asp Ala Thr Pro Val Leu Asn Tyr
 115 120 125
 Asp Leu Leu Tyr Ala Val Ala Lys Leu Gly Pro Gly Glu Lys Tyr Glu
 130 135 140
 Leu His Ala Gly Thr Glu Ser Thr Pro Ser Val Val Val His Val Cys
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 <212> PRT
 <213> Homo sapiens

<400> 7
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 35 40 45
 Glu Phe Leu Gly Lys Glu Met Lys Leu Tyr Phe Ala Gln Thr Leu His
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 Ile Gly Ser Ser His Leu Ala Pro Pro Asn Pro Asp Lys Gln Phe Leu
 65 70 75 80
 Ile Ser Pro Pro Ala Ser Pro Pro Val Gly Trp Lys Gln Val Glu Asp
 85 90 95
 Ala Thr Pro Val Ile Asn Tyr Asp Leu Leu Tyr Ala Ile Ser Lys Leu
 100 105 110

Gly Pro Gly Glu Lys Tyr Glu Leu His Ala Ala Thr Asp Thr Thr Pro
 115 120 125
 Ser Val Val Val His Val Cys Glu Ser Asp Gln Glu Lys Glu Glu Glu
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<210> 8
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 <213> *Cricetulus griseus*

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 Glu Ser Leu Phe Arg Thr Tyr Asp Lys Asp Ile Thr Phe Gln Tyr Phe
 35 40 45
 Lys Ser Phe Lys Arg Val Arg Ile Asn Phe Ser Asn Pro Leu Ser Ala
 50 55 60
 Ala Asp Ala Arg Leu Gln Leu His Lys Thr Glu Phe Leu Gly Lys Glu
 65 70 75 80
 Met Lys Leu Tyr Phe Ala Gln Thr Leu His Ile Gly Ser Ser His Leu
 85 90 95
 Ala Pro Pro Asn Pro Asp Lys Gln Phe Leu Ile Ser Pro Pro Ala Ser
 100 105 110
 Pro Pro Val Gly Trp Lys Gln Val Glu Asp Ala Thr Pro Val Ile Asn
 115 120 125
 Tyr Asp Leu Leu Tyr Ala Ile Ser Lys Leu Gly Pro Gly Glu Lys Tyr
 130 135 140
 Glu Leu His Ala Ala Thr Asp Thr Thr Pro Ser Val Val Val His Val
 145 150 155 160
 Cys Glu Ser Asp Gln Glu Asn Glu Glu Glu Glu Met Glu Arg Met
 165 170 175
 Lys Arg Pro Lys Pro Lys Ile Ile Gln Thr Arg Arg Pro Glu Tyr Thr
 180 185 190
 Pro Ile His Leu Ser
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<210> 9
 <211> 207
 <212> PRT
 <213> *Caenorhabditis elegans*

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 35 40 45
 Ala Asn Phe Ser Ser Leu Phe Thr Gln Ile Glu Lys Asp Ile His Phe
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 Asp Phe Leu Arg Ser Phe Arg Arg Val Arg Val Ile Phe Ser Ser Pro
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 Glu Asn Ala Thr Ala Ala Lys Leu Ile Val Gln Gly Phe Ser Phe Lys
 85 90 95
 Gly His Glu Leu Lys Ala Phe Phe Ala Gln Arg Ile Tyr Met Ser Ala
 100 105 110
 Asn Ser Gln Met Leu Ser Pro Pro Pro Leu Glu Lys Gln Phe Leu Ile
 115 120 125
 Ser Pro Pro Cys Ser Pro Pro Val Gly Trp Glu Gln Thr Lys Asp Met
 130 135 140
 Pro Pro Val Val Cys Asn Phe Asp Leu Met Ala Arg Leu Ala Ser Phe
 145 150 155 160
 Ala Ile Asp Glu Lys Tyr Glu Val His Asn Gly Asp Glu Leu Thr Pro
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 Ala Ile Ile Val His Pro Cys Glu Thr Pro Ile Asp Val Pro Ser Ala
 180 185 190
 Ile Glu Met Pro Arg Thr Pro Arg Pro Ser Ser Pro Cys Glu Gln
 195 200 205

<210> 10
 <211> 211
 <212> PRT
 <213> *Saccharomyces cerevisiae*

<400> 10
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<213> Schizosaccharomyces pombe
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Leu Gly Lys Val Leu Ala Ser Tyr Asn Asp Lys Ala Val Glu Glu Asp
          35                      40                      45

Thr Leu Lys Lys Ser Ser Thr Gly Ser Leu Pro Ser Gly Gln Gln Val
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His Cys Gln Tyr Val Leu Asp Asp Pro Asn His Val Glu Gly Ile Ser
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[illegible]

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<213> Homo sapiens
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<210> 13
<211> 11
<212> PRT
<213> Homo sapiens
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<212> PRT
<213> Homo sapiens
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<400> 14
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<211> 14
<212> PRT
<213> Homo sapiens
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<400> 15
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<210> 16
 <211> 14
 <212> PRT
 <213> Homo sapiens

<400> 16
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 1 5 10

<210> 17
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<400> 17
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<210> 18
 <211> 14
 <212> PRT
 <213> Homo sapiens

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 1 5 10

<210> 19
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 <212> PRT
 <213> Homo sapiens

<400> 19
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<210> 20
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 <212> PRT
 <213> Homo sapiens

<400> 20
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<210> 21
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 <213> Homo sapiens

<400> 21

Pro Lys Pro Lys Ile Asn Gln Thr Arg Arg Pro Gly Leu Pro

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<210> 22

<211> 724

<212> DNA

<213> Mus musculus

<400> 22

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<210> 23

<211> 958

<212> DNA

<213> Mus musculus

<400> 23

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<211> 236

<212> PRT

<213> Mus musculus

<400> 24

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 Lys Glu Arg Phe Glu Ala Leu Phe Thr Leu Tyr Asp Asp Gln Val Thr
 65 70 75 80
 Phe Gln Leu Phe Lys Ser Phe Arg Arg Val Arg Ile Asn Phe Ser Lys
 85 90 95
 Pro Ala Arg Ala Arg Ile Glu Leu His Glu Ser Glu Phe His Gly Arg
 100 105 110
 Lys Leu Lys Leu Tyr Phe Ala Gln Val Gln Val Ser Gly Glu Ala Arg
 115 120 125
 Asp Lys Ser Tyr Leu Leu Pro Pro Gln Pro Thr Lys Gln Phe Leu Ile
 130 135 140
 Ser Pro Pro Ala Ser Pro Pro Val Gly Trp Lys Gln Ser Glu Asp Ala
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 Met Pro Val Ile Asn Tyr Asp Leu Leu Cys Ala Val Ser Lys Leu Gly
 165 170 175
 Pro Gly Glu Lys Tyr Glu Leu His Ala Gly Thr Glu Ser Thr Pro Ser
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 Val Val Val His Val Cys Glu Ser Glu Thr Glu Glu Glu Glu Asp Thr
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<211> 3983

<212> DNA

<213> Mus musculus

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<211> 3717

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<213> Mus musculus

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<210> 28

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: general
calcineurin antagonist peptide

<220>

<221> SITE

<222> (6)

<223> Xaa=any amino acid residue

<400> 28

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<210> 29

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: calcineurin
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<400> 29

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Pro Lys Pro Lys Ile Ile Gln Thr Arg Arg Pro Glu
  1                      5                      10

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<210> 30
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 1 5 10

<210> 31
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 <212> PRT
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<220>
 <223> Description of Artificial Sequence: EGF-derived
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<400> 31
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 1 5 10

<210> 32
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: EGF-derived
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<400> 32
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 1 5 10

<210> 33
 <211> 32
 <212> PRT
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 <223> Description of Artificial Sequence: pH-dependent
 membrane-binding internalizing peptide

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 <222> (1)
 <223> Xaa=preferably a unique residue, such as Cys or
 Lys, that facilitates chemical conjugation of the

internalizing peptide to a targeting protein
conjugate

<220>

<221> SITE

<222> (2)..(3)

<223> Xaa=residues selected to modulate the affinity of
the internalizing peptide for different membranes

<400> 33

Xaa Xaa Xaa Glu Ala Ala Leu Ala Glu Ala Leu Ala Glu Ala Leu Ala
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Glu Ala Leu Ala Glu Ala Leu Ala Glu Ala Leu Glu Ala Leu Ala Ala
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<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: peptide
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<210> 35

<211> 75

<212> DNA

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<221> CDS

<222> (4)..(75)

<220>

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aaa aag aag aga aag gta gct gga ttc 75
Lys Lys Lys Arg Lys Val Ala Gly Phe
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<210> 36
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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: synthetic
 construct

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 1 5 10 15
 Lys Lys Arg Lys Val Ala Gly Phe
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<210> 37
 <211> 225
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: synthetic
 construct

<220>
 <221> CDS
 <222> (4)..(225)

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 Ser Gln Pro Lys Thr Ala Cys Thr Asn Cys Tyr Cys Lys Lys Cys Cys
 20 25 30
 ttt cat tgc caa gtt tgt ttc ata aca aaa gcc ctt ggc atc tcc tat 144
 Phe His Cys Gln Val Cys Phe Ile Thr Lys Ala Leu Gly Ile Ser Tyr
 35 40 45
 ggc agg aag aag cgg aga cag cga cga aga cct cct caa ggc agt cag 192
 Gly Arg Lys Lys Arg Arg Gln Arg Arg Pro Pro Gln Gly Ser Gln
 50 55 60
 act cat caa gtt tct cta agt aag caa gga ttc 225
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 65 70

<210> 38
 <211> 74

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: synthetic construct

<400> 38

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1 5 10 15

Gln Pro Lys Thr Ala Cys Thr Asn Cys Tyr Cys Lys Lys Cys Cys Phe
20 25 30

His Cys Gln Val Cys Phe Ile Thr Lys Ala Leu Gly Ile Ser Tyr Gly
35 40 45

Arg Lys Lys Arg Arg Gln Arg Arg Arg Pro Pro Gln Gly Ser Gln Thr
50 55 60

His Gln Val Ser Leu Ser Lys Gln Gly Phe
65 70

<210> 39

<211> 912

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: synthetic construct

<220>

<221> CDS

<222> (4)..(912)

<400> 39

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1 5 10 15

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Arg Asp Glu Tyr Glu Asp Leu Tyr Tyr Thr Pro Ser Ser Gly Met Ala
20 25 30

agt ccc gat agt ccg cct gac acc tcc cgc cgt ggc gcc cta cag aca 144
Ser Pro Asp Ser Pro Pro Asp Thr Ser Arg Arg Gly Ala Leu Gln Thr
35 40 45

cgc tcg cgc cag agg ggc gag gtc cgt ttc gtc cag tac gac gag tcg 192
Arg Ser Arg Gln Arg Gly Glu Val Arg Phe Val Gln Tyr Asp Glu Ser
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Asp Tyr Ala Leu Tyr Gly Gly Ser Ser Ser Glu Asp Asp Glu His Pro
65 70 75

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Glu Val Pro Arg Thr Arg Arg Pro Val Ser Gly Ala Val Leu Ser Gly	
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Pro Gly Pro Ala Arg Ala Pro Pro Pro Pro Ala Gly Ser Gly Gly Ala	
100 105 110	
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Gly Arg Thr Pro Thr Thr Ala Pro Arg Ala Pro Arg Thr Gln Arg Val	
115 120 125	
gcg act aag gcc ccc gcg gcc ccg gcg gcg gag acc acc cgc ggc agg	432
Ala Thr Lys Ala Pro Ala Ala Pro Ala Ala Glu Thr Thr Arg Gly Arg	
130 135 140	
aaa tcg gcc cag cca gaa tcc gcc gca ctc cca gac gcc ccc gcg tcg	480
Lys Ser Ala Gln Pro Glu Ser Ala Ala Leu Pro Asp Ala Pro Ala Ser	
145 150 155	
acg gcg cca acc cga tcc aag aca ccc gcg cag ggg ctg gcc aga aag	528
Thr Ala Pro Thr Arg Ser Lys Thr Pro Ala Gln Gly Leu Ala Arg Lys	
160 165 170 175	
ctg cac ttt agc acc gcc ccc cca aac ccc gac gcg cca tgg acc ccc	576
Leu His Phe Ser Thr Ala Pro Pro Asn Pro Asp Ala Pro Trp Thr Pro	
180 185 190	
cgg gtg gcc ggc ttt aac aag cgc gtc ttc tgc gcc gcg gtc ggg cgc	624
Arg Val Ala Gly Phe Asn Lys Arg Val Phe Cys Ala Ala Val Gly Arg	
195 200 205	
ctg gcg gcc atg cat gcc cgg atg gcg gcg gtc cag ctc tgg gac atg	672
Leu Ala Ala Met His Ala Arg Met Ala Ala Val Gln Leu Trp Asp Met	
210 215 220	
tcg cgt ccg cgc aca gac gaa gac ctc aac gaa ctc ctt ggc atc acc	720
Ser Arg Pro Arg Thr Asp Glu Asp Leu Asn Glu Leu Leu Gly Ile Thr	
225 230 235	
acc atc cgc gtg acg gtc tgc gag ggc aaa aac ctg ctt cag cgc gcc	768
Thr Ile Arg Val Thr Val Cys Glu Gly Lys Asn Leu Leu Gln Arg Ala	
240 245 250 255	
aac gag ttg gtg aat cca gac gtg gtg cag gac gtc gac gcg gcc acg	816
Asn Glu Leu Val Asn Pro Asp Val Val Gln Asp Val Asp Ala Ala Thr	
260 265 270	
gcg act cga ggg cgt tct gcg gcg tcg cgc ccc acc gag cga cct cga	864
Ala Thr Arg Gly Arg Ser Ala Ala Ser Arg Pro Thr Glu Arg Pro Arg	
275 280 285	
gcc cca gcc cgc tcc gct tct cgc ccc aga cgg ccc gtc gag gaa ttc	912
Ala Pro Ala Arg Ser Ala Ser Arg Pro Arg Arg Pro Val Glu Glu Phe	
290 295 300	

<210> 40
 <211> 303
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: synthetic construct

<400> 40

Met	Thr	Ser	Arg	Arg	Ser	Val	Lys	Ser	Gly	Pro	Arg	Glu	Val	Pro	Arg	1	5	10	15
Asp	Glu	Tyr	Glu	Asp	Leu	Tyr	Tyr	Thr	Pro	Ser	Ser	Gly	Met	Ala	Ser	20	25	30	
Pro	Asp	Ser	Pro	Pro	Asp	Thr	Ser	Arg	Arg	Gly	Ala	Leu	Gln	Thr	Arg	35	40	45	
Ser	Arg	Gln	Arg	Gly	Glu	Val	Arg	Phe	Val	Gln	Tyr	Asp	Glu	Ser	Asp	50	55	60	
Tyr	Ala	Leu	Tyr	Gly	Gly	Ser	Ser	Ser	Glu	Asp	Asp	Glu	His	Pro	Glu	65	70	75	80
Val	Pro	Arg	Thr	Arg	Arg	Pro	Val	Ser	Gly	Ala	Val	Leu	Ser	Gly	Pro	85	90	95	
Gly	Pro	Ala	Arg	Ala	Pro	Pro	Pro	Pro	Ala	Gly	Ser	Gly	Gly	Ala	Gly	100	105	110	
Arg	Thr	Pro	Thr	Thr	Ala	Pro	Arg	Ala	Pro	Arg	Thr	Gln	Arg	Val	Ala	115	120	125	
Thr	Lys	Ala	Pro	Ala	Ala	Pro	Ala	Ala	Glu	Thr	Thr	Arg	Gly	Arg	Lys	130	135	140	
Ser	Ala	Gln	Pro	Glu	Ser	Ala	Ala	Leu	Pro	Asp	Ala	Pro	Ala	Ser	Thr	145	150	155	160
Ala	Pro	Thr	Arg	Ser	Lys	Thr	Pro	Ala	Gln	Gly	Leu	Ala	Arg	Lys	Leu	165	170	175	
His	Phe	Ser	Thr	Ala	Pro	Pro	Asn	Pro	Asp	Ala	Pro	Trp	Thr	Pro	Arg	180	185	190	
Val	Ala	Gly	Phe	Asn	Lys	Arg	Val	Phe	Cys	Ala	Ala	Val	Gly	Arg	Leu	195	200	205	
Ala	Ala	Met	His	Ala	Arg	Met	Ala	Ala	Val	Gln	Leu	Trp	Asp	Met	Ser	210	215	220	
Arg	Pro	Arg	Thr	Asp	Glu	Asp	Leu	Asn	Glu	Leu	Leu	Gly	Ile	Thr	Thr	225	230	235	240
Ile	Arg	Val	Thr	Val	Cys	Glu	Gly	Lys	Asn	Leu	Leu	Gln	Arg	Ala	Asn	245	250	255	

Glu Leu Val Asn Pro Asp Val Val Gln Asp Val Asp Ala Ala Thr Ala
 260 265 270

Thr Arg Gly Arg Ser Ala Ala Ser Arg Pro Thr Glu Arg Pro Arg Ala
 275 280 285

Pro Ala Arg Ser Ala Ser Arg Pro Arg Arg Pro Val Glu Glu Phe
 290 295 300

<210> 41
 <211> 120
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: synthetic
 construct

<220>
 <221> CDS
 <222> (4)..(120)

<400> 41
 cat atg gac gtc gac gcg gcc acg gcg act cga ggg cgt tct gcg gcg 48
 Met Asp Val Asp Ala Ala Thr Ala Thr Arg Gly Arg Ser Ala Ala
 1 5 10 15

tcg cgc ccc acc gag cga cct cga gcc cca gcc cgc tcc gct tct cgc 96
 Ser Arg Pro Thr Glu Arg Pro Arg Ala Pro Ala Arg Ser Ala Ser Arg
 20 25 30

ccc aga cgg ccc gtc gag gaa ttc 120
 Pro Arg Arg Pro Val Glu Glu Phe
 35

<210> 42
 <211> 39
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: synthetic
 construct

<400> 42
 Met Asp Val Asp Ala Ala Thr Ala Thr Arg Gly Arg Ser Ala Ala Ser
 1 5 10 15

Arg Pro Thr Glu Arg Pro Arg Ala Pro Ala Arg Ser Ala Ser Arg Pro
 20 25 30

Arg Arg Pro Val Glu Glu Phe
 35

<210> 43
 <211> 15
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: primer

<400> 43
 aggaggtgga tctgc

15

<210> 44
 <211> 6
 <212> PRT
 <213> Mus musculus

<400> 44
 Glu Arg Met Arg Arg Pro
 1 5

<210> 45
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: consensus
 sequence

<400> 45
 Glu Arg Met Pro Pro Arg Arg Asp
 1 5

<210> 46
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: cross-species
 conserved motif

<220>
 <221> MOD_RES
 <222> (6)
 <223> Variable amino acid

<400> 46
 Leu Ile Ser Pro Pro Xaa Ser Pro
 1 5

<210> 47
 <211> 4

<212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: calcineurin antagonist
 peptide fragment

<220>
 <221> MOD_RES
 <222> (4)
 <223> Any amino acid residue other than Ser or Thr

<400> 47
 Arg Arg Pro Xaa
 1

<210> 48
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: calcineurin antagonist
 peptide fragment

<220>
 <221> MOD_RES
 <222> (4)
 <223> Ala, Gly or Glu

<400> 48
 Arg Arg Pro Xaa
 1

<210> 49
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: calcineurin antagonist
 peptide fragment

<400> 49
 Arg Arg Pro Glu
 1